

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Wright, J.L.C.
Appl. No. : 09/385,834
Filed: : August 30, 1999
Title : A Nutritional Supplement for Lowering
Serum Triglyceride and Cholesterol Level

Grp./A.U. : 1616
Examiner : S. N. Qazi

Docket No. : 76891

DECLARATION PURSUANT TO 37 CFR § 1.132

I, Jaroslav A. Kralovec, M.Eng., Ph.D., hereby declare that:

1. Since 1997, I have been employed by Ocean Nutrition Canada Limited ("ONC"), the assignee of the above-identified application. I am currently the Associate Director of Research, Senior Director of Chemistry. Key details of my employment prior to working with Ocean Nutrition Canada Limited are set forth below:

- 1993-1997 Senior Research Investigator, Chief Chemist - MDS Pharmaceuticals, Toronto, Ontario, and The Institute for Marine Biosciences, National Research Council of Canada, Halifax, Nova Scotia, Canada
- 1987-1993 Senior Research Fellow, Chief Chemist - Dalhousie University, Faculty of Medicine, Department of Biochemistry, Halifax, Nova Scotia, Canada
- 1985-1987 Postdoctoral Research Fellow - Dalhousie University, Faculty of Sciences, Department of Chemistry, Halifax, Nova Scotia, Canada

- 1985 Junior Research Scientist - Research Institute for Pharmacy and Biochemistry, Department of Medicinal Chemistry, Division of AntiCancer Drug Design, Prague, Czechoslovakia

2. Details of my education are as follows:

- 1985 - Ph.D. in Pharmaceutical Chemistry, Research Institute for Pharmacy and Biochemistry, Prague, Scientific College of Czechoslovakia Academy of Sciences
- 1979 - M.Chem.Eng. in Organic Technology, University of Chemical Technology, Prague, Czechoslovakia

3. I have reviewed U.S. patent No. 4,588,717 to Mitchell, which is cited in the final Office Action of July 16, 2003.

4. Mitchell states at column 8, lines 23-33 that:

To form a phytosterol ester in accordance with the present invention, a selected phytosterol and fatty acid are mixed together and allowed to react under conditions which will permit condensation of the phytosterol with the fatty acid to form an ester. For example, by mixing the phytosterol and fatty acid, bringing the mixture to a temperature of from about 15°C to about 45°C at about atmospheric pressure for about 1 to about 3 hours a phytosterol ester will be produced in accordance with the present invention.

5. In examples 1-13, at columns 9-12, Mitchell describes the preparation of phytosterol esters. In each example, the fatty acid used was linoleic acid and the phytosterol was sitosterol, stigmasterol, taraxasterol, or a mixture of two or more thereof.

6. In each of examples 1-13 of Mitchell, the fatty acid and the phytosterol were mixed at room temperature and pressure and allowed to react under these

conditions for one to two hours. Mitchell states in each example that an ester was formed, but does not explain how formation of the ester was determined or detected, nor does he provide any data confirming that an ester was formed.

7. In my opinion, the conditions recited by Mitchell are insufficient to result in a significant degree of esterification. Simply mixing linoleic acid with a phytosterol at room temperature and pressure will result only in a mixture of the fatty acid and the phytosterol. Under these conditions they will produce only insignificant amount of an ester. As discussed below, we conducted an experiment to demonstrate this.

8. On January 6, 2003, Jeffrey H. D. Wright, a research scientist working since 1998 for ONC on phytosterol-PUFA conjugation chemistry, executed an experiment under my supervision in which 720 milligrams of sunflower oil and 50 milligrams of ascorbic acid were mixed for 5 minutes at 40°C. 40°C is at the upper end of the temperature range of 15-45°C recommended by Mitchell.

9. To this mixture was added 250 milligrams of stigmasterol and the resulting mixture was magnetically stirred for two hours and a sample was then taken for thin layer chromatography.

10. The thin layer chromatography of the resulting reaction mixture showed the presence of stigmasterol and the starting oil, but no conversion at all to a steroid ester. TLC system (hexanes/diethylester/acetic acid 9 : 1 : 0.01).

11. These results confirm that simply mixing a phytosterol and a fatty acid or oil containing a fatty acid at room temperature and pressure as described by Mitchell will not result in a significant degree of the reaction of the sterol and the fatty acid to form an ester.

12. I hereby declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under

section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

February 9th, 2004
Date

J. A. Kralovec
Jaroslav A. Kralovec, MEng, Ph.D.,